

Addressing Parents' Concerns About Vaccines

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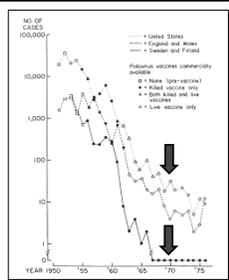


Disclosures

- GlaxoSmithKline, Merck, Novartis, sanofi pasteur
- Ad hoc consultant
- Principal investigator



From Fear of Disease to Fear of Adverse Events



Salk. *Pediatr Infect Dis J* 1987;6:889; *Infectious Disease News*; November, 1998



A Sampling of Anti-Vaccine Groups

- National Vaccine Information Center
- The Alliance for Informed Choice in Vaccination
- Pennsylvania Parents for Vaccine Awareness
- Concerned Parents For Vaccine Safety
- Citizens for Healthcare Freedom
- Vaccine Information Resource Center
- Coalition For Informed Choice
- PAVE: People Advocating Vaccine Education
- Future Generations
- VOICE: Vaccinations- Offering Individuals Choice & Education
- Vaccination Alternatives
- Natural Immunity Information Network
- Ohio Parents for Vaccine Safety
- Healthy Alternatives



Who Are the Vaccine Protestors?

Undervaccinated	Unvaccinated
Black	White
Young, unmarried mother without college degree	Married mother with college degree
Near poverty level	Annual income >\$75,000
Live in central city	Live in states with philosophical exemptions
	Claim doctors have little influence over vaccination decisions

Smith P.J. *Pediatrics* 2004;114:187



Immunization Truths

1. Vaccines are good
2. Public concern about vaccines is pervasive
3. Fear of vaccines can lead to public harm
4. Vaccines are not 100% safe
5. Parents are human
6. People don't understand vaccinology
7. It's all about risk perception
8. There are vaccine anti-champions
9. Questions remain
10. Parents have to make a choice

Marshall. *Infect Dis Child (Suppl)*; Jan, 2003



Vaccine Programs Initiated Before 1980

Disease	Historical Peak		2004-2006	
	Cases	Deaths	Cases	Deaths
Diphtheria	30,508	3,065	0	0
Measles	763,094	552	55	0
Mumps	212,932	50	6,584	0
Pertussis	265,269	7,518	15,632	27
Poliomyelitis (acute)	42,033	2,720	0	0
Poliomyelitis (paralytic)	21,269	3,145	0	0
Rubella	488,796	24	11	0
Congenital rubella synd	20,000	2,160	1	0
Smallpox	110,672	2,510	0	0
Tetanus	601	511	41	4

Roush. JAMA 2007;298:2155

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Vaccine Programs Initiated After 1980

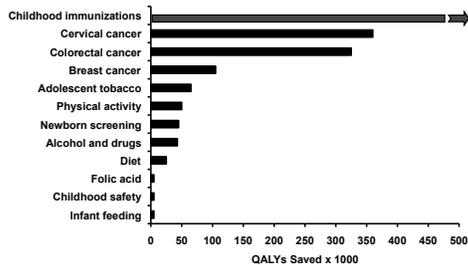
Disease	Historical Peak		2004-2006	
	Cases	Deaths	Cases [†]	Deaths [†]
Hepatitis A	254,518	298	15,298	18
Hepatitis B	74,361	267	13,169	47
Hib (invasive)	>20,000	>1,000	<50	<5
Pneumo (invasive)	64,400	7,300	41,550	4,850
Varicella	5,358,595	138	612,768	19

[†]Estimates

Roush. JAMA 2007;298:2155

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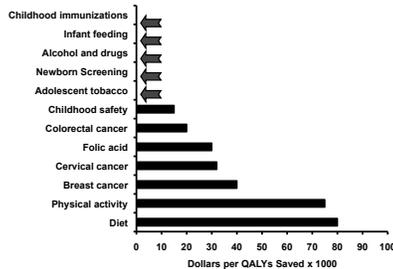
Immunization Truth 1



Coffield. Am J Prev Med 2001;21:1

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Immunization Truth 1



Coffield. Am J Prev Med 2001;21:1

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Immunization Truth 1

Vaccine Programs [†]	2001 Birth Cohort (N=3,803,295)		
	Cases	Deaths	Total Costs
Without	14,330,376	33,564	\$46,557 mil
With	708,372	463	\$482 mil

[†]DtaP, Hib, IPV, MMR, HepB, varicella (not included: rotavirus, HepA, PCV-7, influenza, MCV-4, HPV)

**\$1 spent = \$5 in direct medical costs
\$11 in societal costs**

Zhou F et al. Arch Pediatr Adolesc Med 2005;159:1136-1144

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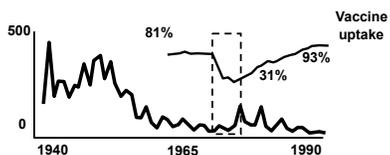
Parental Concerns About Vaccines

Vaccines are a good way to protect children	90%
Generally follow doctor's recommendations	88%
Concerned about adverse effects	54%
Vaccines cause autism	25%
Personally know someone harmed by MMR	40%
Refused at least one recommended vaccine	12%

Freed. Pediatrics 2010;125:654

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Incidence of Pertussis: England and Wales



Gangarosa. Lancet 1998;351:356

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Exemptions and Pertussis Incidence

	Number of States	Adjusted Incidence Rate Ratio (95% CI)
<i>Type of exemption</i>		
Only religious	32	Reference
Personal belief	17	1.48 (1.03-2.13)
<i>Exemption ease</i>		
Difficult	19	Reference
Medium	14	1.35 (0.96-1.91)
Easy	15	1.53 (1.10-2.14)

Omer SB. JAMA 2006;296:1757

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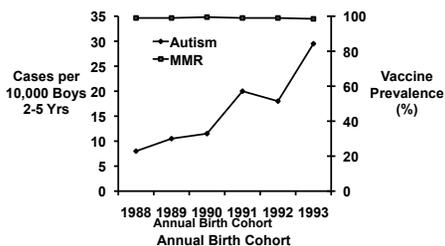
Case-Control Studies

Disease	Risk	Attributable Risk Among Refusers	Attributable Risk in Population
Pertussis	23-times higher	99.5%	11%
Varicella	9-times higher	99.4%	5%

Glanz. Pediatrics 2009;123:1446; Glanz. Arch Pediatr Adol Med 2010;164:66 (Kaiser Permanente, CO)

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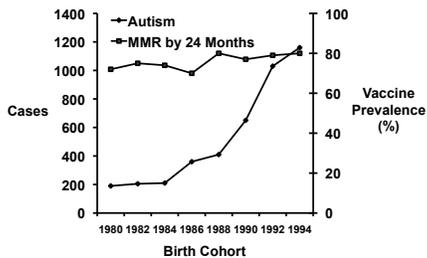
MMR and Autism: United Kingdom



Kaye JA. BMJ 2001;322:460

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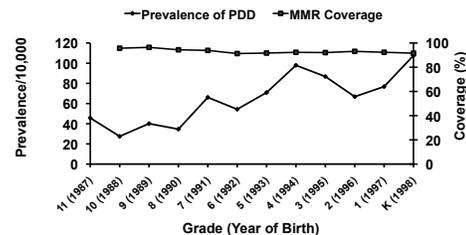
MMR and Autism: California



Dales L. JAMA 2001;285:1183

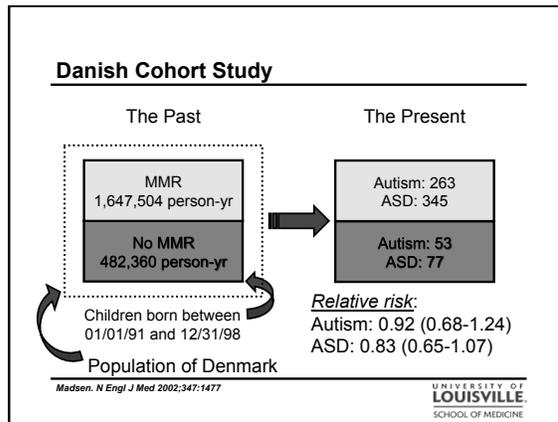
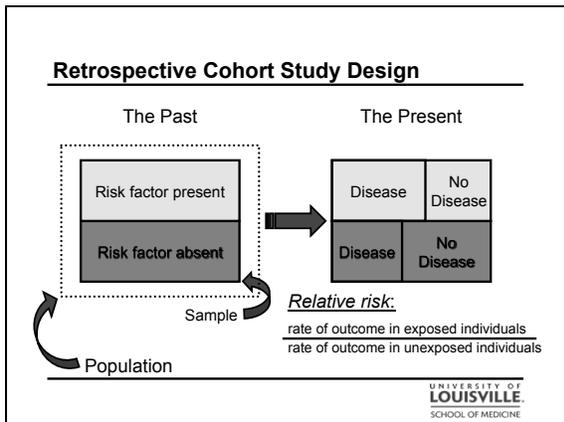
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PDD in Montreal, Canada



Fombonne. Pediatrics 2006;118:e139

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Measles Vaccine and Autism with Enteropathy

- Blinded search for measles RNA using RT-PCR
- 3 separate laboratories
- 25 children with autism and GI disturbances
- 13 children with GI disturbances alone

Study Group	Sex	Age at Biopsy	Time Since MMR	Where Sequences Found	Pathology
Autism	Male	4.7 yr	41 mo	Ileum	RLF
Control	Male	4.0 yr	27 mo	Ileum	RLF

RLF= reactive lymphoid follicles

Hornig. *PLOS* 2008;3:e3140

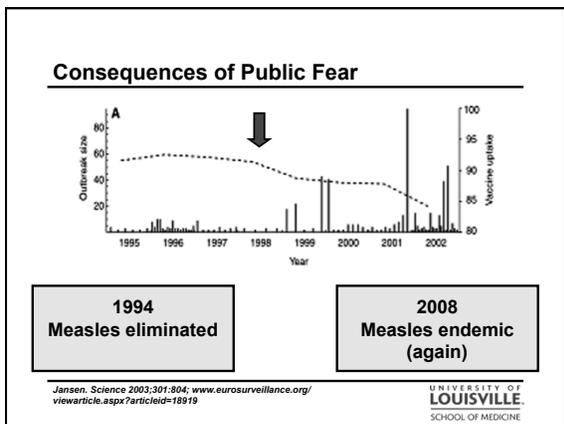
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Wakefield's article linking MMR vaccine and autism was fraudulent

Clear evidence of falsification of data should now close the door on this damaging vaccine scare

Godlee. *BMJ* 2011;342:64

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- ### Measles—United States, January-July 2008
- 131 cases
 - 17 directly imported
 - 99 linked to imported cases
 - 15 link not established
 - 11% hospitalized
 - 123 cases among US residents
 - 80% <20 years of age
 - 91% unvaccinated or vaccination status unknown
 - 66% of eligible individuals not vaccinated because of religious or philosophical beliefs
- CDC. *MMWR* 2008;57:893
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Invasive Hib Disease– Minnesota, 2008

Patient	Age	Syndrome	Outcome	Hib Doses
1	15 mo	Meningitis	Survived [†]	2 mo, 5 mo
2	3 yr	Pneumonia	Survived	0 [‡]
3	7 mo	Meningitis	Died	0 [‡]
4	5 mo	Meningitis	Survived	2 mo, 4 mo
5	20 mo	Epiglottitis	Survived	0 [‡]

[†]Subsequently diagnosed with hypogammaglobulinemia
[‡]Parents or guardians refused vaccination

Highest number of reported cases since 1992

CDC. MMWR 2009;58(ER):Jan 23

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Public Confidence: Vaccine Safety

Marshall. The Vaccine Handbook. PCI Books, Inc.:2008

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Subjects Needed to Test for Increased Risk of Adverse Event Relative to Background Rates[†]

Background rate in general population	Rate in vaccinated population		
	2-fold higher	10-fold higher	100-fold higher
1 in 10,000	141,000	5,500	500
1 in 100,000	1,238,000	53,500	2,500
1 in 1,000,000	12,951,500	532,500	23,500

[†]Assumes 5% risk of Type I error and power of 90%

Evans. J Infect Dis 2009;200:321

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The Power of Box “a”

		Outcome	
		Yes	No
Exposure	Yes	a	b
	No	c	d

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Heuristic Thinking

- Do no harm: a bad outcome is more tolerable if it occurs from inaction rather than action
- Ambiguity: a known risk is more acceptable than an unknown risk
- Availability and representativeness: the probability that something will occur correlates with the ease with which we remember it or with similarity of circumstances
- Compression: rare risks are overestimated and common risks are underestimated

Evans. Risk Comm and Vac. Natl Acad Press, 1997; Ball. Pediatrics 1998;101:453

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Folk Numeracy

- Intuitive sense of numbers that upholds small, anecdotal experiences and makes it difficult to see the big picture
- 10 million women given a shot: 86 will develop optic neuritis within 6 weeks
- 10 million pregnant women given a shot: 16,684 will have a spontaneous abortion within 6 weeks

Shermer M. Sci Amer 2008;Sep;40; Black S. Lancet 2009;374:2115

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Antigen Burden

Vaccine	1960	1980	2000	2010
Smallpox	200			
Diphtheria	1	1	1	1
Tetanus	1	1	1	1
Pertussis	3000	3000	5	5
Polio	15	15	15	15
MMR		24	24	24
Hib			2	2
Varicella			69	69
PCV7/PCV13			8	14
HepB			1	1
HepA				4
HPV4				4
Rotavirus				20
MCV4				5
Influenza				12
Total	3217	3041	126	177

Offit. Pediatrics 2002;109:124 and Marshall. The Vaccine Handbook. PCI Books: 2010

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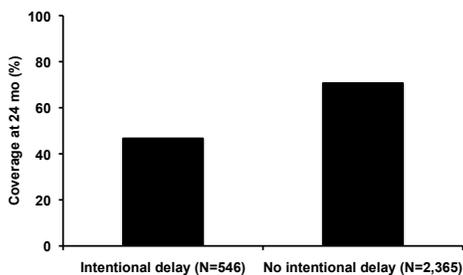
Alternative Vaccine Schedule

	0	1	2	4	6	12	15	18	19-23	2-3	4-6
HepB	→										
Rota	→										
DTaP	→										
Hib	→										
PCV7		→	→	→	→						
IPV		→	→	→	→	→					
Flu				→	→	→					
Measles								→	→	→	→
Varicella								→	→	→	→
HepA									→	→	→

Sears. The Vaccine Book. Little Brown & Co. 2007

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Consequences of Intentional Delay



Smith PJ. Pub Health Rep 2010;125:534

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General Intellectual Functioning

Measure	Untimely (N=556)	Timely (N=491)
Verbal IQ	106.0	108.9
Performance IQ	103.0	107.3
Full-scale IQ	105.3	109.2

Smith MJ. Pediatrics 2010;125:1134 (Wechsler Abbreviated Scale of Intelligence, primary analysis; P<0.05 for each measure)

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Alternative Vaccine Schedule

Parameter	Alternative	ACIP
Total visits to completion	15 visits	4 or 5
Age at completion	42 months	15 or 18 months

Marshall. The Vaccine Quarterly 2009;3[1]:17

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Alternative Vaccine Schedule

Argument	The Truth
Parents can educate themselves to know more than doctors.	Advisory committees are composed of experts who review the primary data.
Government and pharmaceutical companies conspire to misrepresent data.	There is no evidence of conspiracy.
Natural immunity is better than vaccine-induced immunity.	The cost of natural immunity is the risk of serious disease or death.
Vaccines are not adequately tested for safety.	Vaccines are among the most thoroughly tested pharmaceuticals in the world.
Vaccines are recommended for protection of the public, not individuals.	Individuals benefit from vaccines through both individual and herd immunity.
There is a middle ground between causality and coincidence.	Either vaccines do or don't cause certain adverse events.
Science fails because it cannot prove that vaccines don't cause adverse events.	Science can only reject or fail to reject the null hypothesis.

Offit. Pediatrics 2009;123:e164

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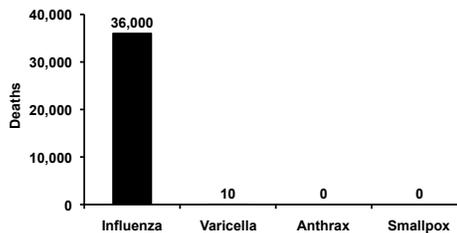
Risk Perception

What We're Afraid Of	What The Real Risk Is
Shark attacks (28)	Dog bites (4.5 million)
Murder (14,180)	Suicide (33,289)
Death by peanut allergy (50)	Death by poisoning (27,531)
Death by plane crash (321)	Death by car crash (34,017)

BLALOCK.ssm.com/abstract=677549; Gigerenzer. Psych Sci 2004;15:286.

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Projected Mortality: U.S., 2011



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The New McCarthyism

- "I have a family history of genetic vulnerability that my kid can't detox vaccines."
- "They say the mercury (thimerosal...) is gone, but it's still in there!"
- "...no wheat, no dairy, because his system can't break them down... it turns them into an opiate making them stoned or drunk...detoxing and occasionally antifungal medicines."
- "It's the pediatrician's fault! Not my fault!"
- "...I'm on an airplane and the pilot comes out to talk to me because his kid is autistic."

US Weekly, Oct 27, 2008

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Cohort Studies of Thimerosal Exposure

Study	Location	Database	Inclusion/Exclusion Criteria	Diagnoses Precisely Defined	Outcome Measures Validated	Appropriate Calculation of Thimerosal Exposure	Control for Bias
Geier 2003	USA	VAERS	No	No	No	No	No
Geier 2003	USA	VAERS DOE	No	No	No	No	No
Geier 2003	USA	VAERS DOE	No	No	No	No	No
Andrews 2004	UK	National Statistics	Yes	Yes	Yes	Yes	Yes
Heron 2004	UK	Avon Long Study	Yes	No	No	Yes	Yes
Hviid 2003	Denmark	National Registries	Yes	Yes	No	Yes	Yes
Verstraeten 2003	USA	HMOs	Yes	Yes	Yes	Yes	No

Parker. Pediatrics 2004;114:793

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Vaccine Adverse Event Reporting System

- Post-marketing surveillance system
- Mandatory reporting by health care providers
 - Events listed as contraindications
 - Events listed in the Reportable Events Table
- Voluntary reporting of any event by any one
- Hypothesis generation not hypothesis testing

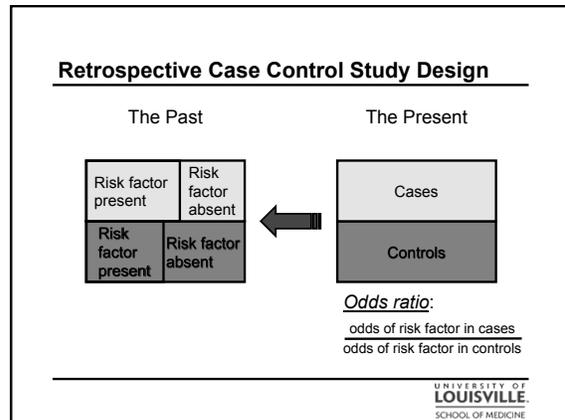
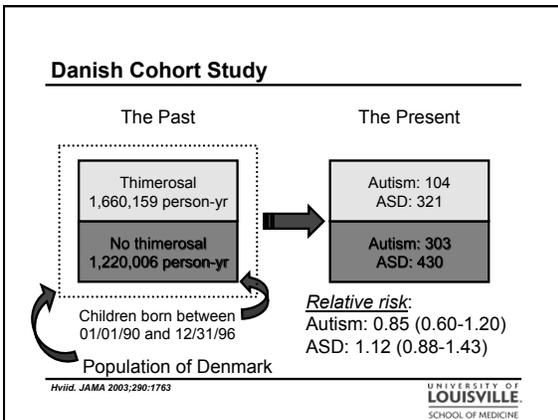
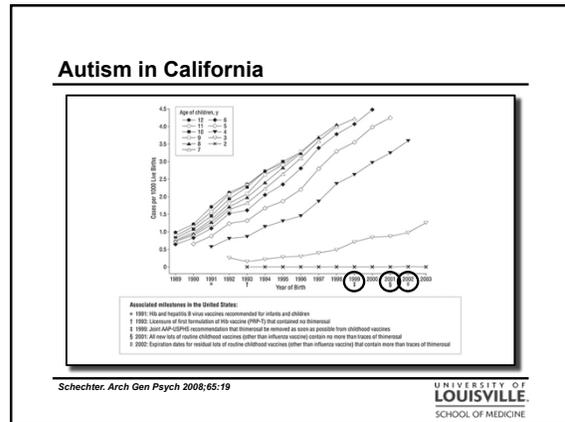
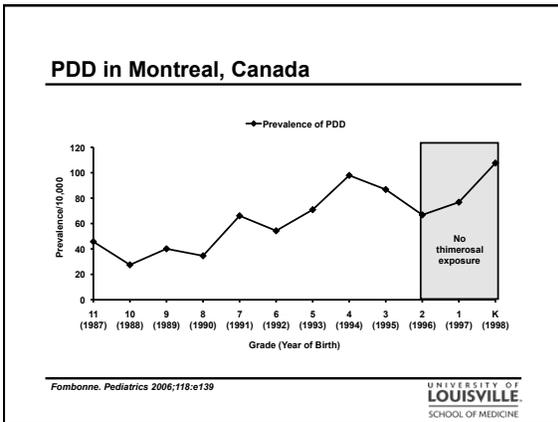
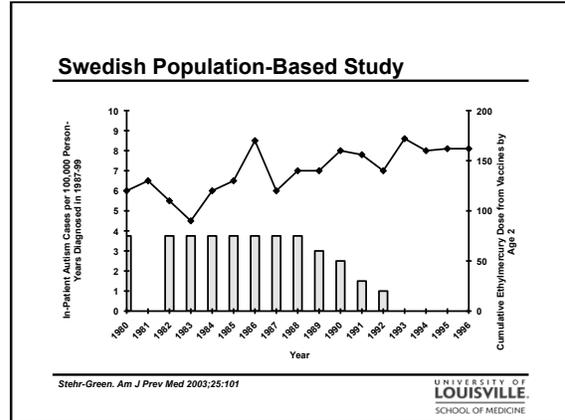
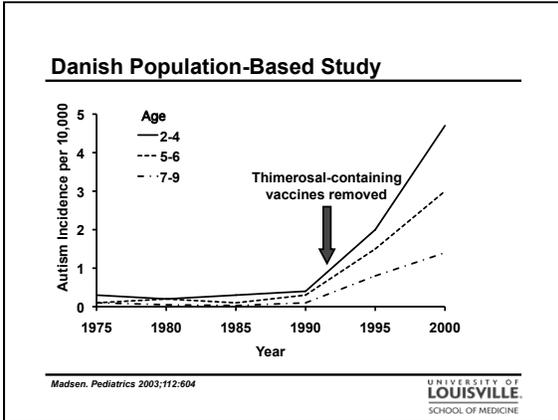
Offit, in Marshall. The Vaccine Handbook. Lippincott Williams & Wilkins, 2004

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VAERS Only Contains Box "a"

		Outcome	
		Yes	No
Exposure	Yes	a	b
	No	c	d

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Vaccine Safety Datalink Study

The Past

Risk factor present	Risk factor absent
Risk factor present	Risk factor absent

Risk factor:
Increase of 1 mcg/kg ethylmercury from birth through 7 mo

The Present

ASD (N=256)
Controls (N=752)

Odds ratio: 0.967
For every 1 mcg/kg increase in exposure, the odds of autism "go up" 0.967

Price. Pediatrics 2010;126:656

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Strengths

- Looked at multiple outcomes
- Looked at prenatal exposures
- Included stakeholders in study design
- Conducted careful individual assessments
- Well-documented exposures
- Surveyed for undiagnosed autism

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Thimerosal Status of Current Vaccines

Vaccine	Trade Name	Manufacturer	Status
Diphtheria, tetanus, pertussis	Infanrix	GlaxoSmithKline	Free
	DAPTACEL	Aventis Pasteur	Free
	Tripedia	Aventis Pasteur	<0.3 mcg/0.5mL
PCV-7	Prevnar	Wyeth	Free
Polio	IPOL	Aventis Pasteur	Free
Hepatitis B	RECOMBIVAX HB	Merck	Free
	Engerix-B	GlaxoSmithKline	Free
Hib conjugate	ActHIB	Aventis Pasteur	Free
	PedvaxHB	Merck	Free
	Hiberix	GlaxoSmithKline	Free
Hib-Hepatitis B	COMVAX	Merck	Free
MMR	M-M-R	Merck	Free
Varicella	VARIVAX	Merck	Free
DTaP/Hep-BSiPV	Pediarix	GlaxoSmithKline	Free
Influenza	Fluzone T-free	sanofi pasteur	Free
	Fluvirin P-free	Chiron/Evans	<1.0 mcg/0.5 mL
	Flumist	MedImmune	Free
Hepatitis A	VAQTA	Merck	Free
	Havrix	GlaxoSmithKline	Free

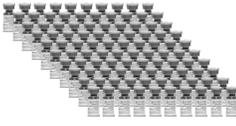
<http://www.fda.gov/Biologics/BloodVaccines/SafetyAvailability/VaccineSafety/UCM096228#11> (accessed 09/01/09)

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Mercury Exposure



5.6 oz
30 mcg



Tripedia
<0.3 mcg/dose

Yess. JAOAC Int'l 1993;76:36

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Aluminum Exposure



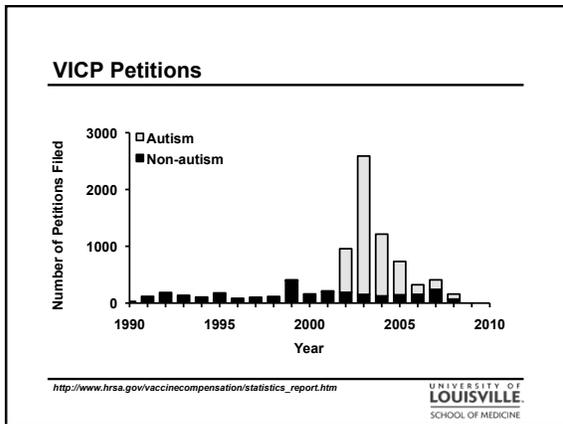
1 L
0.225 mg



ActHIB
0.225 mg/dose

<http://www.chop.edu/service/vaccine-education-center/hot-topics/aluminum.html> (accessed 10/20/09)

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Omnibus Autism Proceedings

- Theories of general causation
 - MMR and thimerosal-containing vaccines combine to cause autism
 - Thimerosal-containing vaccines cause autism
 - MMR causes autism (dropped)
- Three test cases per theory

Magnitude of The Vaccine Court Hearings

- Typical vaccine case
 - 10 medical articles
 - 2-6 experts
- Omnibus Autism Proceedings (Theory 1)
 - 5,000 pages of transcript
 - >700 pages of post-hearing briefs
 - 939 medical articles
 - 50 expert reports
 - Testimony of 28 experts

Theory 1
February 12, 2009



Theory 2
March 12, 2010

Questions

- Which challenges deserve scientific investigation?
- What about perceived conflict of interest?
- How do families differ in medical orientation?
- How should families who refuse to vaccinate be handled?

Parents Have to Choose

Don't vaccinate	Vaccinate
Discredited "scientists"	Robust science
"Advocacy groups"	Authoritative bodies
Celebrities	You
Vulnerability to disease	Protection with minimal risk

**It's not about belief.
It's about science.**